

## Amendments to the Claims

In accordance with 37 CFR 1.121 a Claim Listing is included and the status of each claim is indicated according to the seven permissible status identifiers, i.e. (Original), (Currently amended), (Cancelled), (Previously presented), (New), (Not entered), (Withdrawn). Amended claims use underline for additions and ~~strike-through~~ for deletions.

### Claim Listing:

Claim 1. (Three times amended) A combination therapeutic and diagnostic radiopharmaceutical microparticle comprising a non-radioactive core and at least two different radioactive agents attached to said core, wherein said core is made from a biocompatible polymer, wherein one of said at least two different radioactive agents is a chelated beta-emitting therapeutic radionuclide that is attached to a first terminal functional group of a dendritic polymer linking carrier that is covalently bound to said core, and wherein one of said at least two different radioactive agents is a chelated gamma-emitting diagnostic imaging radionuclide that is attached to a second terminal functional group of a dendritic polymer linking carrier that is covalently bound to said core ~~at least one dendritic polymer linking carrier covalently bound to said core, said dendritic polymer linking carrier having a terminal functional group, said terminal functional group attached to a chelated radiopharmaceutical agent, said chelated radiopharmaceutical agent is selected from the group consisting of a chelated beta-emitting therapeutic radionuclide and a chelated gamma-emitting diagnostic radionuclide.~~

Claim 2-7. (Canceled)

Claim 8. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said therapeutic beta-emitting radionuclide is Yttrium-90.

Claim 9-10. (Canceled)

Claim 11. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said therapeutic beta-emitting radionuclide is Yttrium-90 and said imaging or diagnostic gamma-emitting radionuclide is selected from the group consisting of indium-111 and Tc-99m.

Claim 12. (Three times amended) The radiopharmaceutical microparticle of claim particle of claim 1, ~~further comprising~~ wherein said radioactive therapeutic agent is bonded to said linking carrier through one or more spacer groups.

Claim 13. (Three times amended) The radiopharmaceutical microparticle of claim particle of claim 1, ~~further comprising~~ wherein said dendritic polymer linking carrier is a poly(amidoamine) dendrimer.

Claim 14. (Three times amended) The radiopharmaceutical microparticle of claim particle of claim 13, ~~further comprising~~ wherein said chelator group is at least one selected from the group consisting of cyclohexyldiethylenetriaminepentaacetic acid ligand (CHX-DTPA), diethylenetriaminepentaacetic acid (DTPA), ethylenediaminetetraacetic acid (EDTA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''tetraacetate (DOTA), tetraazacyclotetradecane-N,N'',N'''tetraacetic acid (TETA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O'-bis(-2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), hydroxyethyldiamine triacetic acid (HEDTA), hydroxyethylidene diphosphonate (HEDP), dimercaptosuccinic acid (DMSA), diethylenetriaminetetramethylenephosphonic acid (DTTP) and 1-(p-aminobenzyl)-DTPA, 1,6-diamino hexane-N,N,N',N'-tetraacetic acid, DPDP, and ethylenebis (oxyethylenenitrilo)-tetraacetic acid.

Claim 15. (Three times amended) The radiopharmaceutical microparticle of claim 13, ~~further comprising~~ wherein said therapeutic beta-emitting radionuclide is yttrium-90 and said chelator group is DOTA.

Claim 16. (Cancelled)

Claim 17. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane, polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazine, a poly(vinyl alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, an alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

Claim 18. (Cancelled).

Claim 19. (Cancelled).

Claim 20. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said dendrimer has a disulfide bond in its core.

Claims 21 - 24. (Cancelled)

Claim 25. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said functional group is at least one selected from the group consisting of ester group, ether group, thiol group, carbonyl group, hydroxyl group, amide group, carboxylic group, and imide group.

Claim 26. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said dendrimers are monodispersed.

Claim 27. (withdrawn as non-elected species) The particle of claim 18, wherein said linking carriers are linear polymers.

Claim 28. (withdrawn as non-elected species) The particle of claim 1, wherein said radioactive therapeutic agent is covalently bonded to said linking carrier via a bifunctional linker, carbodiimide condensation, or a disulfid bond formation.

Claim 29. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said particle does not leach radionuclide.

Claim 30. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said particle is spheroidal.

Claim 31. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said particle has a density in the range of from 1 to 4 gm/cm.<sup>sup.3</sup>.

Claim 32. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said particle has a density in the range of from 1 to 2 gm/cm.<sup>sup.3</sup>.

Claim 33. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said particle further comprises a second therapeutic agent or a diagnostic agent.

Claim 34. (Three times amended) The radiopharmaceutical microparticle of claim 33, ~~further comprising~~ wherein said second therapeutic agent or said diagnostic agent is at least one selected from the group consisting of a metal chelate complex, a drug, a prodrug, a radionuclide, a boron addend, a labeling compound, a toxin, a cytokine, a lymphokine, a chemokine, an immunomodulator, a radiosensitizer, an asparaginase, a radioactive halogens, a chemotherapy drug and a contrast agent.

Claim 35. (Twice amended) A particulate material for radiopharmaceutical use comprising microparticles having: a non-radioactive core made from a biocompatible polymer, at least one dendritic polymer linking carrier covalently bound to said core, said dendritic polymer linking carrier having a terminal poly(amidoamine) functional group for attachment to a chelated radiopharmaceutical agent, said chelated radiopharmaceutical agent selected from the group

consisting of a beta-emitting therapeutic radionuclide comprising DOTA-Yttrium-90 and a gamma-emitting diagnostic radionuclide consisting of DOTA-Indium-111 or DOTA-Technetium-99m wherein said linking carrier comprises a biocompatible polymer, and wherein said microparticle has a diameter in the range of from 5 to 200 microns.

Claim 36. (Twice Amended) The particulate material of claim 35, ~~further comprising~~ wherein said microparticles have a diameter in the range of from 8-100 microns.

Claim 37. (Twice Amended) The particulate material of claim 35, ~~further comprising~~ wherein said microparticles have a diameter in the range of from 25-50 microns.

Claim 38. (Twice Amended) The particulate material of claim 35, ~~further comprising~~ wherein said microparticles have a diameter in the range of from 20-30 microns.

Claim 39. (Twice Amended) The particulate material of claim 35, ~~further comprising~~ wherein said microparticles have substantially equivalent particle sizes.

Claim 40. (Twice Amended) The particulate material of claim 35, ~~further comprising~~ wherein said microparticles are sufficiently large so as to avoid phagocytosis.

Claim 41. (withdrawn as non-elected invention) A method of radiation therapy of a patient, which comprises administering to the patient at least one of the microparticles of claim 1, or the particulate material of claim 35-

Claim 42. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said microparticles are administered internally.

Claim 43. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein the administration is direct to a lesion or through a vascular route.

Claim 44. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats cancer or a tumor.

Claim 45. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 44, wherein said cancer is primary or secondary cancer of the liver.

Claim 46. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats a highly vascularized tumor or a tumor which has a single dominant arterial vascular supply.

Claim 47. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 46, wherein said microparticles are injected into an artery supplying a tumor.

Claim 48. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats hepatic cancer, rheumatoid arthritis, a solid cancer, liver cancer, brain cancer, breast cancer and/or ovary cancer.

Claim 49. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats renal cell carcinoma, hepatoma, sarcomas, cancer of the head or neck, and/or a central nervous system tumor.

Claim 50. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said at least one radioactive therapeutic agent is at least one radionuclide selected from the group consisting of an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

Claim 51. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 50, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide and a beta-emitting radionuclide.

Claim 52. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 51, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

Claim 53. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, comprising radiation treatment and imaging or diagnosing.

Claim 54. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is during the life of the radiation.

Claim 55. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is post life of the radiation.

Claim 56. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 51, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

Claim 57. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles are immobilized at a site of administration.

Claim 58. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles do not release a significant amount of radiation emitting radioisotope into the circulation system upon administration.

Claim 59. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 41, wherein said particles have a diameter of from 15 to 35 microns.

Claim 60. (withdrawn as non-elected invention) A kit for preparing a microparticle treatment dose for a patient in need thereof wherein said treatment dose comprises the particulate material of claim 35, wherein said kit comprises particle cores, which do not comprise radionuclide, linkers for attaching at least one radionuclide to said particle cores, and instructions or a means for obtaining instructions for preparing said microparticle treatment dose.

Claim 61. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein said kit contains a radionuclide.

Claim 62. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein a radionuclide is provided separately from said kit.

Claim 63. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of an inert pharmaceutically acceptable carrier, a formulating agent, an adjuvant, an active agent, water, saline, a transfer ligand, a reducing agent, a lyophilization aid, a stabilization aid, a solubilization aid, a bacteriostat, a buffer, an X-ray contrast agent, an ultrasound contrast agent, and a metallopharmaceutical.

Claim 64. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of a syringe, shielding, and imaging equipment.

Claim 65. (withdrawn as non-elected invention) The kit for preparing a microparticle treatment dose of claim 60, wherein said kit comprises multiple types of cores and multiple types of linkers.

Claim 66. (withdrawn as non-elected invention) A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof, determining the type and dosimetry of microparticle treatment needed from a prescription for said patient and preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

Claim 67. (withdrawn as non-elected invention) A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof, determining the type and dosimetry of microparticle treatment needed from a prescription for said patient, selecting a type of core from the cores included in said kit, selecting a type of linker from the linkers included in said kit, selecting a radionuclide and preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

Claim 68. (withdrawn as non-elected invention) The method of claim 60, wherein said microparticle treatment dose is made said kit at a location of administration or at a site proximate

to the location of administration.

Claim 69. (withdrawn as non-elected invention) The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

Claim 70. (withdrawn as non-elected invention) The method of claim 60, wherein said microparticle treatment dose are made said kit at a location of administration or at a site proximate to the location of administration.

Claim 71. (withdrawn as non-elected invention) The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

Claim 72-81. (canceled)

Claim 82. (withdrawn as non-elected invention) A method of radiation therapy of a patient, which comprises administering to the patient microparticles, wherein said microparticles comprise the microparticle as claimed in claim 72.

Claim 83. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 82, comprising radiation treatment and imaging or diagnosing.

Claim 84. (withdrawn as non-elected invention) The method of radiation therapy of a patient of claim 82, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

Claim 85. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said microparticle has a diameter in the range of from about 8 to about 100 microns.

Claim 86. (Three times amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said microparticle has a diameter in the range of from about 20 to about 30 microns.

Claim 87. (Twice Amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said radioactive therapeutic agent is at least one radionuclide selected from the group consisting of iridium, radium, cesium, phosphorus, yttrium, rhenium, actinium, bismuth, astatine, technetium, indium, iodine, and carbon, nitrogen, fluorine, sodium, magnesium, aluminum, silicon, potassium, vanadium, manganese, gallium, niobium, iodine, lead, Y-90, Bi-213, At-211, I-123, I-125, I-131, ~~At-211~~, Cu-67, Sc-47, Ga-67, Rh-105, Pr-142, Nd-147, Pm-151, Sm-153, Ho-166, Gd-159, Th-161, Eu-152, Er-171, Re-186, Re-188, Tc-99m, In-111, ~~Ga-67, Rh-105, I-123, Nd-147, Pm-151, Sm-153, Gd-159, Th-161, Er-171, Re-186, Re-188,~~ and Tl-201.

Claim 88. (Amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein said chelated radiopharmaceutical agent comprises a first radionuclide and a second radionuclide combined on the same microparticle construct, said first radionuclide comprising a chelated beta-emitting therapeutic radionuclide and said second radionuclide comprising a chelated gamma-emitting diagnostic radionuclide.

Claim 89. (Amended) The radiopharmaceutical microparticle of claim 88, ~~further comprising~~ wherein said chelated beta-emitting therapeutic radionuclide comprises Yttrium-90 and said second chelated gamma-emitting diagnostic radionuclide comprises Indium-111 or Technetium-99m.

Claim 90. (Amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein the microparticle is formulated in a pharmaceutical composition in combination with a pharmaceutically acceptable excipient, adjuvant, or carrier.

Claim 91. (Amended) The radiopharmaceutical microparticle of claim 35, ~~further comprising~~ wherein the microparticle is formulated in a pharmaceutical composition in combination with a pharmaceutically acceptable excipient, adjuvant, or carrier.

Claim 92. (Amended) The radiopharmaceutical microparticle of claim 1, ~~further comprising~~ wherein the microparticle is formulated as a lyophilized preparation.

Claim 93. (Amended) The radiopharmaceutical microparticle of claim 35, ~~further comprising~~ wherein the microparticle is formulated as a lyophilized preparation.

Claim 94. (New) The radiopharmaceutical microparticle of claim 1, further comprising a spacer group between the dendritic polymer linking carrier and the chelated radiopharmaceutical agent.

Claim 95. (New) The radiopharmaceutical microparticle of claim 35, further comprising a spacer group between the dendritic polymer linking carrier and the chelated radiopharmaceutical agent.